Reviewer's report

Title: Six sequence variants on chromosome 9p21.3 are associated with a positive family history of myocardial infarction: a multicenter registry

Version: 4 Date: 5 November 2010

Reviewer: Elmo Mannarino

Reviewer's report:

In the present case-control study, 6 common genetic variants at the 9p21.3 locus were all found to be associated with myocardial infarction in men younger than 65 years. The risk was apparently higher for the patients with a positive family history of early coronary heart disease.

The relevance of the 9p21.3 locus as a risk factor for myocardial infarction has been shown in some studies and then confirmed in a number of other investigations. The present study replicates the above findings in a large sample of German people with prevalent myocardial infarction.

1. A limitation of the study is that the control population was not available in the setting of the study, but was selected from 3 previously published populations. This may introduce bias. This limitation should be acknowledged. Moreover, the Authors should provide some more details on the different control populations used. Also, which were the criteria for choosing which specific control population should be matched with the cases for each SNP?

2. The association of SNPs with myocardial infarction in the presence of a positive family history is an interesting aspect of the present study. However, the Authors should try to perform formal interaction tests to see if there is a modifying effect of family history on the relation between the examined SNPs and the risk for myocardial infarction.

Minor issues

The final number of cases included in the study was 976. This should be made clear in the abstract.

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests